June 13, 2005

Recommendations for presumptive treatment of schistosomiasis and strongyloidiasis among the Lost Boys and Girls of Sudan and other Sudanese refugees

SUMMARY

In a recent investigation, a high prevalence of schistosomiasis and strongyloidiasis was found among the Lost Boys and Girls of Sudan. To prevent future morbidity from these diseases, the Centers for Disease Control and Prevention (CDC) recommends that Sudanese refugees should receive pre-departure presumptive treatment for schistosomiasis and strongyloidiasis. Additionally, all members of the Lost Boys and Girls of Sudan and other Sudanese refugees from similar circumstances who have resettled to the U.S. should receive presumptive treatment for schistosomiasis and strongyloidiasis. The regimens for presumptive treatment are the same whether they are given overseas or after arrival to the U.S. (Figure 1). Treatment for schistosomiasis should consist of praziquantel (Biltricide®) at a dose of 20 mg/kg, given in two oral doses 6-8 hours apart for refugees at least 4 years of age. For Lost Boys and Girls and other Sudanese refugees from similar overseas circumstances[1] who are at least 1 year of age, treatment of strongyloidiasis should consist of albendazole (Albenza®) at a dose of 400 mg, given in oral doses, twice a day for 7 days. This document provides background

[1] For the remainder of this document, Lost Boys and Girls refugees and other Sudanese refugees who have been in similar overseas circumstances will be referred to as "Sudanese refugees".

information on the investigation, rationale for the recommendations, and technical information for physicians.

BACKGROUND

CDC recently conducted an epidemiologic investigation of schistosomiasis and strongyloides among the Lost Boys and Girls of Sudan (http://www.cdc.gov/ncidod/dq/lostboysandgirlssudan/presumptive_tx_recc.htm). Serologic testing for these parasitic diseases was performed by CDC Division of Parasitic Diseases.[2] The investigation identified a high prevalence of these parasitic infections. Among the 462 Lost Boys and Girls of Sudan who were tested, 203 (44%) tested positive for schistosomiasis, and 214 (46%) tested positive for strongyloidiasis. Overall, 103 (22%) of Lost Boys and Girls were seropositive for both schistosomiasis and strongyloidiasis, and 315 (69%) were seropositive for either parasitic infection. Immunoblot testing was performed on 21 randomly selected ELISA positive persons; 12 (57%) were infected with *Schistosoma mansoni*, 2 (9%) were infected with *S. haematobium*, 4 (19%) were infected with both, and 3 (14%) were infected with neither.

Before departure from Africa, U.S.-bound refugees ages 2 years and older currently receive one oral dose of albendazole (600 mg). Although albendazole is effective against many parasitic infections, this dosage of albendazole is inadequate to treat

[2] The tests performed were CDC ELISA serologic tests. The schistosomiasis test is 99% and 90% sensitive in detecting antibodies to *Schistosoma mansoni* and *S. haematobium*, respectively. The test for strongyloidiasis is 95% sensitive in detecting antibodies to *Strongyloides stercoralis*. While the sensitivity and specificity of stool tests for either schistosomiasis or strongyloidiasis and urine tests for *S. haematobium* can vary depending on the number and technique of the tests performed, these CDC serologic tests have much greater sensitivity. Both these tests are available only at CDC; no locally available serologic tests for schistosomiasis or strongyloidiasis have known reliability.

strongyloides and does not provide any coverage for schistosomiasis. Without treatment, both schistosomiasis and strongyloidiasis can lead to significant morbidity, such as liver failure from chronic schistosomiasis infection and the hyperinfection syndrome in immunocompromised persons with strongyloidiasis infection. Therefore, even asymptomatic persons with these parasitic infections should be treated.

RECOMMENDATIONS

Based on the high prevalence of schistosomiasis and strongyloides and to prevent future morbidity from these diseases among others who were not tested, CDC recommends modifications to the pre-departure and post-arrival presumptive treatment protocols. Thus, for Sudanese refugees, CDC recommends the following:

1) The modification of the current pre-departure presumptive intestinal parasite treatment for Sudanese refugees to include adequate treatment for schistosomiasis and strongyloidiasis.

2) The administration of post-arrival presumptive treatment among Sudanese refugees who did not receive pre-departure treatment.

PRESUMPTIVE PRE-DEPARTURE TREATMENT

Figure 1 provides a summary of the recommendations for Sudanese refugees. The recommended treatment for schistosomiasis is praziquantel at a dose of 20 mg/kg, given in two oral doses 6-8 hours apart given to refugees at least 4 years of age.

While ivermectin (Stromectol®) is considered the drug of choice for treatment of strongyloidiasis, CDC is not recommending this drug for presumptive treatment for strongyloidiasis in Sudanese refugees because of concerns about potential concurrent *Loa loa* infection (a filarial parasite transmitted by the tabanid fly in Western and Central Africa). Persons who have high levels of *Loa loa* microfilaremia may have a life-threatening encephalopathic reaction if treated with ivermectin. Thus, ivermectin should not be given to Sudanese refugees unless *Loa loa* microfilaremia has been ruled out. The preferable method of diagnosis of *Loa loa* infection is a daytime blood smear for circulating microfilariae performed by an experienced laboratorian. Antibody testing for filiarial infections can also be performed at the National Institutes of Health (Dr. T. B. Nutman; 301-496-5398). Because the prevalence of *Loa loa* infection among Sudanese refugees is unknown and testing for *Loa loa* is not widely available, CDC recommends that Sudanese refugees at least 1 year of age receive an extended regimen of albendazole (400 mg, given in oral doses, twice a day for 7 days days), which does not cause adverse reactions in persons infected with *Loa loa*. If a Sudanese refugee has been tested for *Loa loa* infection and is negative, that refugee should receive ivermectin at a dose of 200 mcg/kg in one oral dose if weight ≥15 kg. Refugees receiving ivermectin to treat strongyloidiasis should also receive, if greater than 1 year of age, albendazole, 600 mg in one oral dose (to treat other intestinal parasites not treated by ivermectin).

Recommendations were previously developed and distributed regarding presumptive treatment of schistosomiasis and strongyloidiasis among the Lost Boys and Girls of Sudan who had been resettled to the U.S. (http://www.cdc.gov/ncidod/dq/lostboysandgirlssudan/presumptive_tx_recc.htm). In those recommendations, albendazole at a dose of 400 mg, given in oral doses, twice a

day for 3 days was recommended to treat strongyloidiasis. Since the development of those recommendations, an updated Medical Letter[3] has recommended 7 days of albendazole therapy to treat strongyloidiasis while the current Sanford Guide[4] recommends 2 days of albendazole therapy. Each of these published recommendations is the result of a consensus between experts. The optimal duration of albendazole to treat strongyloidiasis is unknown. However, many experts believe that a longer duration of albendazole may yield higher cure rates. While ivermectin is the drug of choice for strongyloidiasis, neither ivermectin nor albendazole (of any duration) consistently provide cure rates of 100%.

Refugees who have been treated for strongyloidiasis with 3 days of albendazole do not necessarily need to be re-treated with additional albendazole. The difference in efficacy between 3 days and 7 days of therapy is unknown. If physicians are concerned about whether or not 3 days of albendazole was curative, repeat strongyloidiasis serologic testing can be performed 6 months after therapy through the Division of Parasitic Diseases (770-488-7775).

Praziquantel, albendazole, and ivermectin may be administered concurrently (WHO, oral communication).

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[3] The Medical Letter. Drugs for parasitic infections. http://www.medicalletter.org/freedocs/parasitic.pdf.

[4] The Sanford Guide to Antimicrobial Therapy 2005, 35th Edition. Editors Gilbert DN, Moellering RC, Eliopoulos GM, Sande MA. Hyde Park: Antimicrobial Therapy, Inc., 2005, p 98.

PRESUMPTIVE POST-ARRIVAL TREATMENT

All Sudanese refugees who resettled prior to implementation of these recommendations should receive praziquantel and albendazole as described in the recommendations for pre-departure treatment (Figure 1). Sudanese refugees who received pre-departure treatment with albendazole (600 mg in one oral dose) should also receive the recommended extended albendazole therapy (400 mg, oral doses, twice a day for 7 days).

Refugees who were ineligible to receive presumptive therapy for schistosomiasis and strongyloidiasis at the time of resettlement should receive presumptive therapy for schistosomiasis and strongyloidiasis when they reach the appropriate age and weight. As with pre-departure presumptive treatment, praziquantel, albendazole, and ivermectin may be administered concurrently.

PRECAUTIONS AND CONTRAINDICATIONS TO PRESUMPTIVE TREATMENT

Presumptive treatment should be administered to all refugees, except for the following circumstances. For many of these circumstances, testing for schistosomiasis and strongyloidiasis is presented as an option. Testing for schistosomiasis and strongyloidiasis can consist of stool (for *S. mansoni* or strongyloidiasis) or urine (*S. haematobium*) examinations. Physicians ordering testing should be aware that the CDC serologic tests are more sensitive than either stool or urine examinations. Thus, urine and stool microscopy tests for these parasitic diseases cannot be used to rule out infection and serologic testing should be considered for patients who test negative by stool and urine microscopy.

1. Children

Children under 1 year of age should not receive presumptive treatment. Children greater than 1 year of age can receive albendazole therapy. Children under 4 years of age should not receive praziquantel. Children weighing less than 15 kg should not receive ivermectin. However, there has been extensive overseas use of these medications during World Health Organziation (WHO) helminth control activities. For overseas situations in which therapy for children may otherwise be indicated, the Division of Global Migration and Quarantine should be contacted. For post-arrival situations, CDC's Division of Parasitic Diseases should be consulted (770-488-7775). Physicians should be aware that serologic testing for children can be performed through the Division of Parasitic Diseases (770-488-7775).

For overseas refugee children who do not meet the minimum age or weight requirements for presumptive therapy, the need for subsequent treatment should be indicated on the appropriate Immigration Health Assessment form (DS Form #2053).

2. Pregnant women

Praziquantel is a pregnancy category B drug, while ivermectin and albendazole are pregnancy category C drugs. Women of childbearing age who may be pregnant should have a negative pregnancy test prior to administration of these medications.

Presumptive overseas pre-departure treatment for pregnant women should be deferred until after delivery. Any instances of pregnant women who are immunocompromised prior to pregnancy or have clinical signs and/or symptoms of disease should be discussed with clinicians in the Division of Global Migration and Quarantine. For pregnant women who are overseas, the need for subsequent treatment after delivery should be indicated on the appropriate immigration health assessment form (DS Form #2053).

For pregnant women who have arrived in the U.S., presumptive treatment can be deferred until after delivery. Alternatively, serologic tests can be performed at CDC and a decision about treatment for women who test positive can be made in conjunction with clinicians from CDC's Division of Parasitic Diseases (770-488-7775). Pregnant women who are immunocompromised should be tested for schistosomiasis and strongyloides at CDC.

3. Women who are breastfeeding

Praziquantel can be administered to lactating women, but the milk should be discarded for 72 hours following treatment with praziquantel. Ivermectin is excreted in human milk in low concentrations. Mothers who intend to breast feed should be treated with ivermectin only when the risk of delayed treatment to the mother outweighs the risk to the newborn. Because it is unknown whether albendazole is excreted in human milk, caution should be exercised when albendazole is administered to a lactating woman.

Pre-departure presumptive treatment for lactating women can be delayed until they are no longer breastfeeding. Although these medications can be administered to lactating women under certain considerations, concerns about the safety of alternative milk supplies overseas justify the postponement of presumptive treatment. For immunocompromised women who are lactating and lactating women who have clinical signs and/or symptoms of disease, decisions about treating these women overseas should be made in consultation with clinicians from the Division of Global Migration and Quarantine. For lactating women who are overseas, the need for subsequent treatment should be indicated on the appropriate immigration medical examination form (DS Form #2053).

For lactating women who have arrived in the U.S., presumptive treatment may be postponed until they are no longer breastfeeding. Alternatively, lactating women can also be tested with serologic tests performed at CDC; decisions about treatment for women who test positive, immunocompromised women who are lactating, and lactating women who have clinical signs and/or symptoms of disease can be made in consultation with clinicians from CDC's Division of Parasitic Diseases (770-488-7775).

4. Refugees who are immunocompromised[5]

Refugees who are immunocompromised, including refugees with AIDS, HIV infection, cancer, chronic steroid users, and persons who have had an organ

[5] Except women who are pregnant or breastfeeding. See previous discussion regarding pregnant and lactating women.

transplant or who may receive an organ transplant, should receive presumptive treatment for schistosomiasis and strongyloides (Figure 1). Serologic testing of immunocompromised refugees is not necessary prior to treatment. However, physicians wishing to test immunocompromised refugees prior to therapy may do so through the Division of Parasitic Diseases (770-488-7775). While follow-up testing for schistosomiasis or strongyloidiasis is not routinely necessary after completion of presumptive therapy, immunocompromised patients should have serologic testing for strongyloides performed at CDC six months after treatment. No additional tested is required for schistosomiasis. Additional information about strongyloides testing is available at CDC's Division of Parasitic Diseases (770-488-7775).

5. Refugees with cysticercosis infection

Persons who have cysticercosis infection may have seizures following treatment with praziquantel, ivermectin, or albendazole because these medications can kill *Taenia solium* cysticerci, thus provoking seizure activity. The prevalence of cysticercosis among African refugees is believed to be low based on the known geographic distribution of cysticercosis. Refugees with a history of seizures who have not been evaluated for cysticercosis should be evaluated before receiving these drugs. Refugees with cysticercosis should not receive presumptive treatment and should have serologic testing for schistosomiasis and strongyloidiasis performed at CDC. Physicians with questions regarding cysticercosis infection and its evaluation can consult clinicians from CDC's Division of Parasitic Diseases (770-488-7775).

6. Refugees with a seizure disorder not evaluated for cysticercosis

   Patients with a seizure disorder that have not been evaluated for cysticercosis should be evaluated before receiving these drugs. Refugees who have a history of cysticercosis or are pregnant should not receive presumptive treatment and should have serologic testing for schistosomiasis and strongyloidiasis performed at CDC. Refugees who test positive for either of these infections should have a treatment plan developed in coordination with a physician.

Physicians should consult the package inserts for additional information about praziquantel, ivermectin, and albendazole. Additional background information on the investigation among the Lost Boys and Girls, rationale for the recommendations, and technical information for clinicians is available at http://www.cdc.gov/ncidod/dq/lostboysandgirlssudan/presumptive_tx_recc.htm.

POST-TREATMENT RECOMMENDATIONS AND FOLLOW-UP

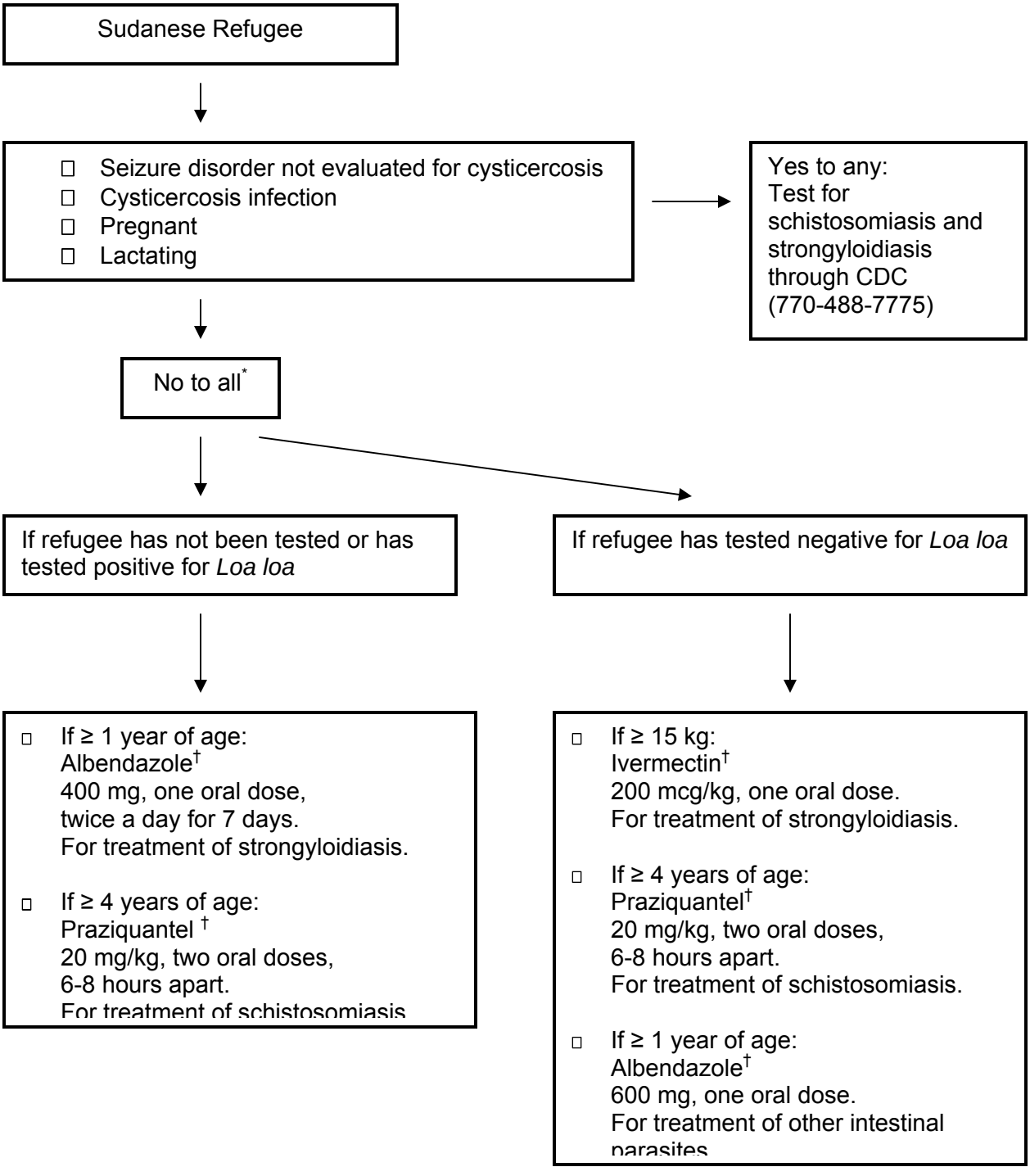
Follow-up testing for schistosomiasis or strongyloidiasis is not routinely necessary after presumptive treatment for these diseases is completed. However, persons who have symptoms that suggest failure of cure or morbidity from these diseases should have appropriate follow-up testing performed. Such patients should be under the care of a physician; CDC physicians are available to provide guidance in these situations.

In addition, persons who are immunocompromised or may become immunocompromised in the near future, including persons with AIDS, HIV infection, cancer, chronic steroid users, and persons who have had a transplant or who may

receive a transplant are at high risk for *Strongyloides* hyperinfection syndrome. All refugees who have been treated should be counseled about this risk, and refugees who are immunocompromised should seek follow-up care with their primary physician. Although routine follow-up testing is not necessary for immunocompetent refugees, immunocompromised persons should have a serologic test for *Strongyloides* performed by CDC at least 6 months after treatment to ensure cure has occurred. All refugees should be counseled that if they become immunocompromised in the future, *Strongyloides* testing should be performed at that time to rule out ongoing strongyloidiasis. CDC can provide additional consultation as needed for these patients or patients for whom presumptive therapy may have failed.

For questions regarding these recommendations, please contact Dr. Drew Posey (404-498-1601; dposey@cdc.gov) or Dr. Michelle Weinberg (404-498-1652; mweinberg@cdc.gov) at the Division of Global Migration and Quarantine.

Figure 1. Presumptive treatment of schistosomiasis and strongyloidiasis among Sudanese refugees.



* Immunocompromised refugees can be tested prior to treatment, and any refugee who later becomes immunocompromised would need strongyloidiasis testing 6 months after receiving therapy.

† Albendazole, praziquantel, and ivermectin can be administered concurrently.